Docket No.: 249692001700
(PATENT)

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Patent Application of:
Alain H. CURAUDEAU et al.

Application No.: 10/588,419

Confirmation No.: 8347

Filed: February 8, 2005 (Int'l)

Art Unit: 1614

For: PHOTODYNAMIC THERAPY FOR THE TREATMENT OF HYPERACTIVE SEBACEOUS GLAND DISORDERS USING TOPICALLY APPLIED HYDROPHOBIC GREEN PORPHYRINS

Examiner: D. Jagoe

DECLARATION OF VALERY RUBINCHIK UNDER 37 C.F.R. § 1.132

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Dear Madam:

I, Valery Rubinchik, declare as follows:

1. I am one of the co-inventors of the above-referenced application, and am familiar with the contents thereof.

2. I am Senior Director, Device Technology at QLT. Inc., the assignee of the present application. I am experienced in and remain actively engaged in the field of pharmaceutical research and development. A copy of my *curriculum vitae* is attached hereto as Exhibit A.

3. I have reviewed the final Office action mailed September 2, 2009 and the references cited therein. This declaration is submitted in response to the final Office action, to distinguish the present invention from the cited art.

4. The sole independent claim of the present invention, claim 1, relates to a photodynamic therapy (PDT) method for the treatment of hyperactive sebaceous gland disorders. Claim 1 requires topically administering a hydrophobic and/or lipophilic photosensitizer composition to the affected skin tissue of a subject, and then irradiating with a wavelength of light suitable to activate the photosensitizer at a fluence rate between about 0.1 mW/cm^2 and about 600 mW/cm^2.

5. The cited reference to Candela Corporation (WO 2003/086460) discloses high fluence rate PDT methods for treating dermatologic conditions while minimizing or preventing side effects, such as purpura of the treated skin, "based on the surprising discovery that a high fluence rate can be used for effective treatment while the overall fluence is kept below the purpura threshold." (See WO 2003/086460 at page 4, lines 16-19.) Candela Corporation further discloses that "[t]he findings that pulsed irradiation can be advantageous for ALA-PDT is also surprising in light of the current understanding of the mechanism of action of photodynamic therapy. Not only are the total light doses as used in the current invention lower than those that have been used to successfully treat skin lesions in the past, but the fluence rates are considerably higher." (See WO 2003/086460 at page 6, lines 10-13.)

6. Candela Corporation describes irradiation with light having "a wavelength between about 500 nm and about 650 nm, a fluence rate between about 100 W/cm^2 and about 40 MW/cm^2, and a fluence of less than about 60 J/cm^2." (See WO 2003/086460 at page 4, lines 25-27.) Typical fluence rates are described as including the following ranges: about 100 W/cm^2 to about 40 MW/cm^2; about 300 W/cm^2 to about 30 MW/cm^2; about 500 W/cm^2 to about 20 MW/cm^2, and about 500 W/cm^2 to about 10 MW/cm^2. (See WO 2003/086460 at page 15, lines 14-18.)

7. In maintaining the obviousness rejection, the Office asserts that the range of fluence rates recited in the present claims overlaps with the range of fluence rates disclosed by Candela Corporation. The Office's position requires interpreting the recitation of "a fluence rate between about 100 W/cm^2 and about 40 MW/cm^2" to mean "a fluence rate between about 100 watts per square centimeter and about 40 milliwatts per square centimeter." In view of the disclosure of Candela Corporation as a whole, this interpretation is unsupportable.

8. A milliwatt is defined as "[a] unit of power equal to one-thousandth of a watt. Abbreviated mW." (McGraw-Hill Dictionary of Scientific and Technical Terms, 6th Edition, 2003, page 1345; attached as Exhibit B). A megawatt is defined as "[a] unit of power, equal to 1,000,000 watts. Abbreviated MW." (McGraw-Hill Dictionary of Scientific and Technical Terms, 6th Edition, 2003, page 1305; attached as Exhibit C). The use of these conventions when referring to units of power is standard in the art.

9. In discussing light sources used in conventional PDT methods, Candela Corporation explicitly refers to "fluence rates of 10 to 500 milliwatts per square centimeter (mWcm^{-2})" (emphasis added), and the reference consistently uses this abbreviation when discussing fluence rates used in conventional PDT methods known in the art, demonstrating that the drafters were familiar with the convention of referring to units of milliwatts as "mW." (See WO 2003/086460 at page 1, lines 25-26; see also page 2, lines 4-28.) Similarly, Candela Corporation consistently refers to units of "MW/cm^2" when referring to the high fluence rates used in their invention. (See WO 2003/086460 at page 15, lines 14-18.) The consistent usage of two different abbreviations, mW and MW, when referring to conventional and high fluence rate methods, respectively, clearly suggests that these terms are not equivalent, as presupposed by the Office.

10. Exemplary conditions described by Candela Corporation include the use of a 595 nm pulsed dye laser at a fluence of 10 J/cm^2 for about 10 ms (comprised of multiple short pulses), to achieve a fluence rate of about 20 MW/cm^2. (See WO 2003/086460 at page 15, lines 18-20). Even a single 10 ms laser pulse at a fluence of 10 J/cm^2 provides a fluence rate of 1000 W/cm^2. Thus, the stated fluence rate of "20 MW/cm^2" cannot reasonably be understood to refer to 20 milliwatts per

square centimeter (i.e., 0.02 W/cm^2). Candela Corporation also discloses that a flashlamp can be used to achieve a desired fluence rate, in the range of from about 500 W/cm^2 to about 1000 W/cm^2. (See WO 2003/086460 at page 15, lines 23-24.)

11. In describing the unexpected efficacy of their methods, Candela Corporation states that "a 10 millisecond (ms) laser pulse with a fluence of 7.5 Jcm^{-2} corresponds to a fluence rate of 750 Wcm^{-2}. This fluence rate is more than 3 orders of magnitude greater than the fluence rates used in conventional ALA-PDT. However, this fluence rate is well below the peak fluence rate value of $4 \times 10^4 Wcm^{-2}$ which is the estimated threshold for a reduction in PDT efficacy due to saturation." (See WO 2003/086460 at page 6, lines 27-31).

12. In view of the disclosure that the theoretical peak fluence rate is $4 \times 10^4 Wcm^{-2}$, i.e., 40 kW/cm^2, it is reasonable to infer that the "40 MW/cm^2" upper limit for the fluence rates referred to by Candela Corporation was intended to refer to 40 kW/cm^2. However, regardless of the intended upper limit, it is clear that the lower limit of the high fluence rate range envisaged by Candela Corporation is 100 W/cm^2, more than two orders of magnitude greater than the claimed upper limit of 600 mW/cm^2 (i.e., 0.6 W/cm^2), as recited in the pending claims.

13. As understood by those of ordinary skill in the art, PDT is a photochemical reaction that requires light, photosensitizer and oxygen. The results are dependent on the ability of photons of light to collide with drug molecules in the presence of oxygen, to produce oxygen radicals which in turn interact with tissue cells causing apoptosis or necrosis, depending on PDT dose. In the case of continuous wave (CW) light, there is a steady supply of photons. Provided the fluence rate is properly selected to match the amount of oxygen in the treated area, controlled and predictable PDT results. In the case of pulsed light, short peaks (milliseconds) of very high light intensity are provided, separated by periods of no light. As a result of having abundance of light (high fluence rate) for a very short period of time, a lot of photons are "wasted" in pulsed light methods, due to a lack of sufficient drug and/or oxygen to interact with. On the other hand, the periods of no light allow for the tissue to re-oxygenate, leading to more effective PDT when the light is on. Thus, even

in cases where the cumulative light dose is the same for pulsed versus CW PDT, those of skill in the art understand that the outcome of treatment is usually different and somewhat difficult to predict.

14. I declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further, that these statements are made with the knowledge that willful, false statements and the like so made are punishable by fine or imprisonment or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

Executed at Vancouver, B.C., Canada, on December 22'09

V. Rubinchik

Valery Rubinchik, MSc.